Applicants: GÖPFERICH, Achim et al.

U.S. Nat. Ph.: PCT/EP00/06313

Serial No: 10/019,797

## **Status of the Claims**

Att. Docket MB9962P

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

1. (Currently Amended) A linear block copolymer, comprising the structure c2)-b)-c1)-a), wherein:

the a) is a hydrophobic biodegradable polymer a), the hydrophobic polymer a) being selected from one or more of polylactide, polyglycolide, poly(lactide-co-glycolide), poly-β-hydroxybutyrate and poly-β-hydroxyvalerate;

the b) is a hydrophilic polymer b) comprising polyethylene glycol;

the c1) is a first functional end group c1) bound directly to <u>and linking</u> the hydrophobic polymer a) to the hydrophobic biodegradable polymer a); and

the c2) is a primary amino group, second functional end group c2) not bound to, but capable of covalently binding, a surface-modifying substance d) to the hydrophilic polymer b) by way of an at least bifunctional molecule, wherein said second functional end group c2) is neither a hydroxyl group nor a carboxylic acid and wherein the at least bifunctional molecule, when bound to the copolymer, has at least one free functional end group that is different from the second functional end group c2) and that is capable of covalently binding with the surface-modifying substance d), and wherein the structure of the copolymer permits binding the copolymer-linked bifunctional reagent to the surface modifying substance d) without substantial loss of bioactivity of such substance in an instant reaction at room temperature with a solution or suspension comprising the surface-modifying substance d).

2. (Currently Amended) The block copolymer of Claim 1, wherein: the-first functional end group c1) is an end hydroxyl group; and the second functional end group c2) is a primary amino group.

GÖPFERICH, Achim et al. Applicants: Att. Docket MB9962P

U.S. Nat. Ph.: PCT/EP00/06313

Serial No: 10/019,797

3. (Previously Presented) The block copolymer of Claim 2, wherein the hydrophilic polymer b) is poly(ethylene glycol) amine (PEG-NH2).

#### 4. Cancelled.

5. (Previously Presented) The block copolymer of Claim 1, wherein the hydrophilic polymer b) is at least one polymer selected from the group consisting of polyethylene glycol, polypropylene glycol, polyethylene glycol/polypropylene glycol copolymer, polyethylene glycol/polypropylene glycol/polyethylene glycol copolymer, polybutylene glycol, polyacrylamide, polyvinyl alcohol, polysaccharide, peptide and protein.

## 6-8. Cancelled.

- 9. (Previously Presented) The block copolymer of Claim 1, wherein the polyethylene glycol has a molar mass in a range of 200 to 10,000 Da.
- 10. (Previously Presented) The block copolymer of claim 1, wherein the hydrophobic polymer a) is polylactide with a molar mass in a range of 1,000 to 100,000 Da.
- 11. (Currently Amended) The block copolymer of claim 1, wherein the surface of the block copolymer is <u>covalently</u> <del>characterized by</del> bound <u>to</u> surface-modifying substances d).
- 12. (Previously Presented) The block copolymer of Claim 1, wherein the block copolymer additionally contains at least one surface-modifying substance d), wherein substance d) is bonded to the hydrophilic polymer b) by means of the reactive group c).

U.S. Nat. Ph.: PCT/EP00/06313 Serial No: 10/019,797

(Previously Presented) The block copolymer of Claim 12, wherein the substance d) is at least one substance selected from a carbohydrate, peptide, protein, heteroglycan, proteo-glycan, glycoprotein, amino acid, fat, phospholipid, glycolipid, lipoprotein, medicinal agent, antibody, enzyme, DNA/RNA, a cell, dye and molecular sensor.

- (Previously Presented) A shaped body formed from the block copolymer of Claim 1.
- (Previously Presented) The shaped body of Claim 14, wherein the shaped body is a film, particle, three-dimensional body, porous body or a sponge.
- 16. (Withdrawn) The use of a block copolymer according to Claim 1 for the production of drug-targeting systems, drug-delivery systems, bioreactors, for therapeutic and diagnostic purposes, for tissue engineering and as emulsifier.
- 17. (Withdrawn) The process for the production of a block copolymer of Claim 12, wherein the at least one substance d) is converted with a block copolymer according to Claim 1, wherein the block copolymer is present in solution or in the solid phase.
- 18. (Withdrawn) The process according to Claim 17, wherein for binding the at least one substance d), the block copolymer according to Claim 1 is used in the form of a porous shaped body.

U.S. Nat. Ph.: PCT/EP00/06313 Serial No: 10/019,797

Scriai No. 10/019,797

19. (Withdrawn) The process for the production of a block copolymer according to Claim 12, wherein in a first stage, the substance d) is provided with a reactive group c) and in a second stage, the complex composed of substance d) and reactive group c) is bonded by means of the reactive group c) to the hydrophilic polymer b) of a block copolymer composed of a hydrophobic polymer a) and a hydrophilic polymer b).

- 20. (Withdrawn) The process for the production of a block copolymer according to Claim 12, wherein the binding of the at least one substance d) to the surface of the block co-polymer is achieved by generating a substrate pattern, and the reactive group c) is selected from 1) an at least bifunctional molecule with at least one free functional group and/or 2) a functional group.
- 21. (Withdrawn) The process according to Claim 20, wherein the substance d) is applied with a locally constant or variable concentration by means of the reactive group c) on the surface of a block copolymer containing a hydrophobic component a) and hydrophilic component b).
- 22. (Withdrawn) The process according to Claim 20, wherein for binding the reactive group c) and/or the substance d) in a substrate pattern, the surface of the block copolymer is structured by a plotter, an ink jet printer, radiation with light, bombardment with particles, stamping or soft lithography.

U.S. Nat. Ph.: PCT/EP00/06313

hydrophobic polymer a) and a hydrophilic polymer b).

Serial No: 10/019,797

23. (Withdrawn) The process for the production of a block copolymer according to Claim 13, wherein in a first stage, the substance d) is provided with a reactive group c) and in a second stage, the complex composed of substance d) and reactive group c) is bonded by means of the reactive group c) to the hydrophilic polymer b) of a block copolymer composed of a

- 24. (Withdrawn) The process for the production of a block copolymer according to Claim 17, wherein in a first stage, the substance d) is provided with a reactive group c) and in a second stage, the complex composed of substance d) and reactive group c) is bonded by means of the reactive group c) to the hydrophilic polymer b) of a block copolymer composed of a hydrophobic polymer a) and a hydrophilic polymer b).
- 25. (Withdrawn) The process for the production of a block copolymer according to Claim 18, wherein in a first stage, the substance d) is provided with a reactive group c) and in a second stage, the complex composed of substance d) and reactive group c) is bonded by means of the reactive group c) to the hydrophilic polymer b) of a block copolymer composed of a hydrophobic polymer a) and a hydrophilic polymer b).
- 26. (Withdrawn) The process for the production of a block copolymer according to Claim 13, wherein the binding of the at least one substance d) to the surface of the block co-polymer is achieved by generating a substrate pattern, and the reactive group c) is selected from 1) an at least bifunctional molecule with at least one free functional group and/or 2) a functional group.

U.S. Nat. Ph.: PCT/EP00/06313 Serial No: 10/019,797

functional group.

27. (Withdrawn) The process for the production of a block copolymer according to Claim 17, wherein the binding of the at least one substance d) to the surface of the block co-polymer is achieved by generating a substrate pattern, and the reactive group c) is selected from 1) an at least bifunctional molecule with at least one free functional group and/or 2) a

- 28. (Withdrawn) The process for the production of a block copolymer according to Claim 18, wherein the binding of the at least one substance d) to the surface of the block co-polymer is achieved by generating a substrate pattern, and the reactive group c) is selected from 1) an at least bifunctional molecule with at least one free functional group and/or 2) a functional group.
- 29. (Withdrawn) The process according to Claim 26, wherein the substance d) is applied with a locally constant or variable concentration by means of the reactive group c) on the surface of a block copolymer containing a hydrophobic component a) and hydrophilic component b).
- 30. (Withdrawn) The process according to Claim 27, wherein the substance d) is applied with a locally constant or variable concentration by means of the reactive group c) on the surface of a block copolymer containing a hydrophobic component a) and hydrophilic component b).
- 31. (Withdrawn) The process according to Claim 28, wherein the substance d) is applied with a locally constant or variable concentration by means of the reactive group c) on the surface of a block copolymer containing a hydrophobic component a) and hydrophilic component b).

U.S. Nat. Ph.: PCT/EP00/06313

Serial No: 10/019,797

32. (Withdrawn) The process according to Claim 21 wherein for binding the reactive group c) and/or the substance d) in a substrate pattern, the surface of the block copolymer is structured by a plotter, an ink jet printer, radiation with light, bombardment with particles, stamping or soft lithography.

- (Previously Presented) The block copolymer of Claim 1, wherein the hydrophobic polymer a) is polylactide with a molar mass greater than 1,000 Da.
  - 34. Cancelled.
  - 35. Cancelled.
- 36. (Previously Presented) The block copolymer of Claim 1, wherein the second functional end group is for binding of a surface-modifying substance d) to the hydrophilic polymer b) either directly or by way of an at least bifunctional molecule with at least one free functional end group.
- 37. (Previously Presented) The block copolymer of Claim 1, wherein the second functional end group is for binding of a surface-modifying substance d) to the hydrophilic polymer b) either directly or by way of an at least bifunctional molecule, the at least bifunctional molecule having at least one free functional end group that is bound or suitable for being bound with the surface-modifying substance d).

U.S. Nat. Ph.: PCT/EP00/06313 Serial No: 10/019,797

38. (Previously Presented) The block copolymer of Claim 1, wherein the second

functional end group is for covalent binding of a surface-modifying substance d) directly to the

hydrophilic polymer b).

39. Cancelled.

40. Cancelled.

41. (Previously Presented) The block copolymer of Claim 1, wherein the second

functional end group is for covalent binding of a surface-modifying substance d) to the

hydrophilic polymer b) by way of an at least bifunctional molecule, the at least bifunctional

molecule having at least one free functional end group that is not bound but suitable for being

bound with the surface-modifying substance d).

42. (Previously Presented) The block copolymer of Claim 41, wherein the least one

free functional end group is different from the second functional end group.

43. (Previously Presented) The block copolymer of Claim 1, wherein the second

functional end group is for binding of a surface-modifying substance d) to the hydrophilic

polymer b) by way of an at least bifunctional molecule, the at least bifunctional molecule having

at least one free functional end group that is covalently bound to the surface-modifying

substance d).

44. (Previously Presented) The block copolymer of Claim 43, wherein the least one

free functional end group is different from the second functional end group.

Page 9 of 22

U.S. Nat. Ph.: PCT/EP00/06313

Serial No: 10/019,797

#### 45-62. Cancelled.

# 63. (Withdrawn) A block copolymer, comprising:

a hydrophilic biodegradable polymer a) comprising one or more compounds selected from the group consisting of polylactide, polyglycolide, poly(lactide-co-glycolide), poly-β-hydroxybutyrate and poly-β-hydroxyvalerate, wherein each a) comprises at least two first functional end groups c1),

wherein each end group c1) participates in a covalent bond with a proximal end of a hydrophilic polymer b) comprising polyethylene glycol, and

wherein at a distal end of each b) is a c2), which comprises a second functional end group c2) capable of covalently binding a surface-modifying substance d) to the hydrophilic polymer b), and wherein second functional end group c2) is neither a hydroxyl group nor a carboxylic acid.

#### 64. Cancelled.

- 65. (Withdrawn) A population of molecules in aqueous medium comprising the structure a)-c1)-b)-c2), wherein:
- a) is a surface comprising a hydrophobic biodegradable polymer, the hydrophobic polymer a) being joined to said surface and selected from one or more of polylactide, polyglycolide, poly(lactide-co-glycolide), poly-β-hydroxybutyrate and poly-β-hydroxyvalerate;
  - b) is a hydrophilic polymer comprising polyethylene glycol;
- c1) is a first functional end group of hydrophobic polymer a) which is covalently bound to hydrophilic polymer b); and

U.S. Nat. Ph.: PCT/EP00/06313 Serial No: 10/019,797

c2) comprises a second functional end group c2) capable of covalently binding a surface-modifying substance d) to the hydrophilic polymer b), wherein said second functional end group c2) is neither a hydroxyl group nor a carboxylic acid, and

wherein the orientation each the molecule is such that hydrophilic component b) and second functional end group c2) project out from said surface, comprising said hydrophobic polymer a), thereby facilitating the binding of surface modifying substance d).

- 66. (Withdrawn) The block co-polymer molecule of claim 63, wherein the surface is insoluble in the aqueous medium.
  - 67. (Currently Amended) A substantially linear block co-polymer, comprising:
- a) a <u>biodegradable</u> hydrophobic block comprising at least one hydrophobic polymer <del>covalently bound at a proximal end to a surface</del>; and
- b) a hydrophilic block comprising at least one hydrophilic polymer covalently bound to the hydrophobic block, wherein a distal end of the hydrophilic block contains a terminal reactive primary amine group which excludes a carboxyl; wherein the reactive group is suitable for forming a covalent bond, via a linking bifunctional reagent with a surface modifying substance in aqueous solution or suspension, and wherein the structure of the copolymer permits binding the copolymer-linked bifunctional reagent to the surface modifying substance without substantial loss of bioactivity of such substance in an instant reaction at room temperature with said solution or suspension.
- 68. (Currently Amended) The block co-polymer of claim 67, wherein[[:]] the hydrophobic block comprises one or more polymers containing polylactic acid, polyglycolic acid, or a mixture of lactic acid and glycolic acid moieties, <u>and</u> the hydrophilic block comprises a <u>modified</u> polyethylene glycol <u>monoamine</u> having an amino group, the block co-polymer has a

U.S. Nat. Ph.: PCT/EP00/06313 Serial No: 10/019,797

reactive group other than a carboxyl, and the reactive group is suitable for forming a covalent-bond at a distal terminus with a surface modifying substance.

69. (Currently Amended) The block co-polymer of claim 68, wherein the hydrophobic block comprises polylactic acid and wherein the hydrophilic block comprises poly-(ethanolamine ethylene glycol-monoamine) monoamine (PEG-NH<sub>2</sub>).

70. (Previously Presented) The block co-polymer of claim 69, wherein the hydrophobic block has a molecular weight of 100-100,000 Da and the hydrophilic block contains from a single ethanolamine to a poly(ethanolamine) having a molecular weight of about 10,000 Da.

71. (New) A substantially non-immunogenic linear block copolymer, comprising the structure c2)-b)-c1)-a), wherein:

the a) comprises a polylactide component;

the b) comprises a polyethylene glycol component;

the c1 is a hydroxyl group linking a) and b); and

the c2 is a primary amine which can bind a surface-modifying substance d) to the hydrophilic polymer b) by way of an at least bifunctional molecule; the at least bifunctional molecule selected from the group consisting of disuccinimidyl tartaric acid and disuccinimidyl succinate, wherein the structure of the copolymer permits binding the copolymer-linked bifunctional reagent to the surface modifying substance d) in an instant reaction with a solution or suspension comprising the surface-modifying substance d).

U.S. Nat. Ph.: PCT/EP00/06313 Serial No: 10/019,797

72. (New) The block co-polymer of claim 71, wherein the hydrophobic block has a molecular weight of from about 100 to about 100,000 Da and the hydrophilic block contains from a single ethanolamine to a PEG-NH<sub>2</sub> moiety having a molecular weight of from about 1000 to about 10,000 Da.

73. (New) The block copolymer of claim 71 having a structure as follows:

$$H = \begin{bmatrix} CH_3 \\ O \end{bmatrix} \begin{bmatrix} O \\ D \end{bmatrix} \begin{bmatrix} O \\ M \end{bmatrix} \begin{bmatrix} O \\ M$$

wherein n is at least about 19 and m is at least about 5.

74. (New) The block co-polymer of claim 71, wherein the polylactide moiety has a maximum molar mass of about 100,000 Da and the PEG moiety has a maximum molar mass of about 10,000 Da.